

## CLAIMS

1. A betacellulin mutein or a salt thereof, wherein the pancreatic  $\beta$  cell differentiation promoting activity is preserved, and the epithelial cell growth promoting activity is reduced.

2. A betacellulin mutein or salt thereof according to Claim 1, wherein the ratio of the pancreatic  $\beta$  cell differentiation promoting activity to the epithelial cell growth promoting activity is at least twice relative to that of betacellulin.

3. A betacellulin mutein or salt thereof according to Claim 1, wherein 1 to 40 amino acid residues from the N terminal of the betacellulin may be deleted, and 1 to 4 amino acid residues of the first through fourth amino acid residues from the C terminal, including the Leu at 3 from the C terminal and the Asp at 4 from the C terminal, may be deleted or substituted with other amino acid residues or other peptide chains.

4. A betacellulin mutein or salt thereof according to Claim 3, wherein 1 to 40 amino acid residues from the N terminal have been deleted.

08857815.060301

09857815-060801

5. A betacellulin mutein or salt thereof according to Claim 3, comprising (1) an amino acid sequence represented by SEQ ID NO: 1, (2) an amino acid sequence in which 1 to 40 amino acids from the N terminal in the amino acid sequence represented by SEQ ID NO: 1 have been deleted, (3) an amino acid sequence represented by SEQ ID NO: 2, or (4) an amino acid sequence in which 1 to 40 amino acids from the N terminal in the amino acid sequence represented by SEQ ID NO: 2 have been deleted.

6. A betacellulin mutein or salt thereof according to Claim 3, comprising (1) an amino acid sequence represented by SEQ ID NO: 1, (2) an amino acid sequence represented by SEQ ID NO: 2, (3) an amino acid sequence represented by SEQ ID NO: 3, or (4) an amino acid sequence represented by SEQ ID NO: 4.

7. A betacellulin mutein or salt thereof according to Claim 3, comprising (1) an amino acid sequence represented by SEQ ID NO: 37, or (2) an amino acid sequence represented by SEQ ID NO: 38.

8. A betacellulin mutein or salt thereof according to Claim 1, wherein 1 to 30 amino acid residues from the N terminal of the betacellulin may be deleted, and 1 to 5 amino acid residues may be inserted between the 22<sup>nd</sup> and 23<sup>rd</sup> amino acid residues from the C terminal.

9. A betacellulin mutein or salt thereof according to Claim 8, wherein 1 to 30 amino acid residues from the N terminal of the betacellulin have been deleted.

10. A betacellulin mutein or salt thereof according to Claim 8, comprising the amino acid sequence represented by SEQ ID NO: 44.

11. A betacellulin mutein or salt thereof according to Claim 8, comprising the amino acid sequence represented by SEQ ID NO: 45.

12. A method for manufacturing a betacellulin mutein or salt thereof according to Claim 1, characterized by culturing the transformants which have been transformed with recombinant vectors containing DNA encoding the betacellulin mutein according to Claim 1 to produce said betacellulin mutein.

13. A pharmaceutical composition comprising a betacellulin mutein or salt thereof according to Claim 1.

14. A pharmaceutical composition according to Claim 9, wherein the composition is a prophylactic or therapeutic drugs for diabetes.

09857815-060801

15. A method for prophylaxis or treatment for diabetes, characterized in that a betacellulin mutein or salt thereof according to Claim 1 is administered to mammals.

16. The use of a betacellulin mutein or salt thereof according to Claim 1 to manufacture a prophylactic or therapeutic agent for diabetes.

09857815-060801